

The warning criterion of intraoperative bulbocavernosus reflex monitoring in adult patients with lumbosacral intraspinal tumor

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Abstract

Objective: There are currently no standard warning criteria for intraoperative neurophysiological monitoring (IONM) of bulbocavernosus reflex (BCR). This study aimed to preliminarily detect a practical warning criterion for use in intraoperative BCR monitoring in adult patients with lumbosacral intraspinal tumor. **Methods:** Adult patients with lumbosacral intraspinal tumor who underwent surgery with BCR monitoring were recruited. Patients were classified into four groups according to the amplitude decline rate of BCR responses at the end of surgery compared with the baseline: Group 1, <50%; Group 2, ≥50% and <75%; Group 3, ≥75% and <100%; Group 4, 100% (BCR disappeared). The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for three specified cutoff values of BCR amplitude decline rate at 50%, 75% and 100% to predict postoperative voiding function were calculated. Receiver operating characteristic curve analysis was used to determine the optimal cutoff value of BCR amplitude decline. Voiding function was evaluated based on subjective urinary symptoms and postvoid residual urine volume measurement at 1 month post-operatively. **Results:** A total of 57 patients were included in the study. There were 33 (57.9%) males and the mean age was (51.2±15.3) years. There were 46 patients (26 males) in Group 1, 3 patients (2 males) in Group 2, 3 patients (1 male) in Group 3, and 5 patients (4 males) in Group 4. Two patients (2 males) in Group 1, 1 patient (0 male) in Group 2, 2 patients (0 male) in Group 3, and 4 patients (4 males) in Group 4 demonstrated worsened voiding function at 1 month post-operatively. When the warning criterion of BCR amplitude decline rate was set as 50%, the sensitivity, specificity, PPV, and NPV of BCR monitoring for worsened voiding were 77.8%, 91.7%, 63.6%, and 95.7% respectively. When the warning criterion was 75%, the sensitivity, specificity, PPV, and NPV were 66.7%, 95.8%, 75.0%, and 93.9% respectively. When the warning criterion was 100%, the sensitivity, specificity, PPV, and NPV were 44.4%, 97.9%, 80.0%, and 90.4% respectively. According to the ROC curve analysis, the optimal cutoff value of BCR amplitude decline for predicting voiding function at 1 month post-operatively was 66.5%. The area under curve, sensitivity, and specificity were 0.813, 77.8% and 95.8% respectively. **Conclusions:** Intraoperative BCR monitoring is a valuable tool to be performed during surgery in adult patients with lumbosacral intraspinal tumor. The cutoff value of BCR amplitude decline rate at 100% (all or none criterion) can be used to predict postoperative voiding function, and the absence of BCR is a robust indication for poor voiding post-operatively. As a warning criterion, the cutoff value of BCR amplitude decline at 66.5% may be practical.

Keywords: bulbocavernosus reflex, intraoperative neurophysiological monitoring, voiding function, lumbosacral intraspinal tumor, warning criterion, receiver operating characteristic curve analysis

INTRODUCTION

Surgery for lumbosacral intraspinal tumor

carries a relatively high risk of postoperative voiding difficulty, making it essential to utilize

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Date of Submission: 1 August 2024; Date of Acceptance: 8 October 2024

<https://doi.org/10.54029/2025upk>

intraoperative neurophysiological monitoring (IONM) to assess and monitor the voiding function in real time throughout the procedure. The bulbocavernosus reflex (BCR) is a somatic polysynaptic spinal reflex mediated by the S2-S4 spinal cord segments.¹⁻³ The afferent somatic sensory pathway of the BCR includes the dorsal penile/clitoral nerve, the pudendal nerve, the sacral plexus, and sacral roots of S2-S4. The efferent somatic motor pathway comprises the motor neurons in Onuf's nucleus, sacral roots of S2-S4, the pudendal nerve, the sacral plexus, the deep branch of the pudendal nerve, and the bulbocavernosus and external sphincter muscles.⁴ The advantage of BCR monitoring is that it enables the clinicians to directly observe the functional integrity of the sacral reflex circuit, which is essential for the maintenance of normal voiding and sexual function. Any damage to the afferent or efferent pathways or the reflex center in sacral spina cord can be detected by BCR. Thus, intraoperative BCR monitoring is expected to play a critical role in helping to preserve preoperative urinary function in surgery for lumbosacral intraspinal tumor. Moreover, surgeons need not interrupt their surgery, as both stimulation and recording are performed outside of the surgical field.⁵ The BCR included two components⁶⁻⁷: the early oligosynaptic response (R1) and the late polysynaptic response (R2). As R1 is remarkable for lack of habituation under general anesthesia, it is routinely used for data analysis in IONM.

After the groundbreaking work conducted by Deletis and Vodusek in 1997⁵, a few studies had demonstrated intraoperative BCR monitoring was feasible to reduce the risk of postoperative voiding dysfunction in lumbosacral intraspinal surgery, especially in pediatric tethered cord syndrome.⁸⁻¹³ To the best of our knowledge, it has not been widely used in adult patients with lumbosacral intraspinal tumor¹⁴⁻¹⁶ and there are no standard warning criteria for BCR monitoring. Hence, this study is aimed to preliminary detect a practical warning criterion for use in intraoperative BCR monitoring in adult patients with lumbosacral intraspinal tumor.

The contents of this study mainly include two parts: first, amplitude reduction from 50%-100% has been used as alert criteria for other INOM procedures such as somatosensory evoked potential (SSEP) and motor evoked potential (MEP).¹⁷⁻¹⁹ We selected three specified cutoff values of BCR amplitude decline rate at 50%, 75% and 100% according to SSEP and MEP to assess the diagnostic value respectively. Second, receiver operating characteristic (ROC) curve

analysis was performed to determine an acceptable warning criterion in BCR monitoring.

METHODS

Subjects

Patients over 18 years old at surgery who were diagnosed with lumbosacral intraspinal tumor and received IONM with BCR during operation in the Neurological Disease Center of Peking University International Hospital from May 2021 to April 2024 were recruited. MRI showing lesions at or under the level of the 10th thoracic vertebrae meet the inclusion criteria. The final diagnosis was based on the pathological reports. Exclusion criteria were: (1) preoperative urinary catheter insertion; (2) bilateral absence of the baseline of BCR; (3) failure to complete the follow-up. The study was approved by the Medical Ethics Committee of Peking University International Hospital (2023-KY-0064-01).

Intraoperative BCR monitoring

Sevoflurane was used for inhalation induction and intravenous anesthesia was maintained by propofol and remifentanyl. No additional skeletal muscular relaxants were administered after tracheal intubation to avoid pharmacological effects on BCR as much as possible. Bispectral index (BIS) indicating the depth of anesthesia was adjusted to maintain in 40-60 range.

A certified neurophysiological technician performed the IONM throughout the surgery. The BCR monitoring was performed according to the protocol described by Deletis and Vodusek⁵ using the JB-116B (NIHON KOHDEN CORP., Tokyo, Japan) system. Surface electrodes were used for the stimulation. In males, a pair of electrodes were placed on the dorsal side of the penis with the proximal part as the cathode and the distal part as the anode. In females, the electrodes were placed on the clitoris as the cathode and the labia majora as the anode. For BCR recording, two pairs of needle electrodes were inserted into the external anal sphincters on bilateral sides. The intensity of stimulation was required to generate a recordable BCR waveform (approximately 2-50 mA). The parameters of BCR stimulation were list as follows: Biphasic 8-pulse constant-current stimulation, duration 0.3ms, pulse interval 3.0ms, frequency 2.3Hz. The baseline of BCR was obtained after the dura mater was opened and the BCR recording was performed at regular intervals during surgery.

Grouping and voiding function evaluation

Patients were classified into four groups according to the amplitude decline rate of BCR responses at the end of surgery compared with the baseline: Group 1, <50%; Group 2, ≥50% and <75%; Group 3, ≥75% and <100%; Group 4, 100% (BCR disappeared). Since the BCR was recorded on both sides of the anal sphincter, the amplitude decline rate of the prominent side was used for data analysis.

Voiding function was evaluated based on subjective urinary symptoms and postvoid residual urine volume measurement at 1 month post-operatively. Urinary symptoms were assessed according to the core lower urinary tract symptom score (CLSS) questionnaire described by Homma *et al.*²⁰ The questionnaire selected 10 of 25 symptoms defined by the International Continence Society Standardization Committee. The CLSS questionnaire was collected via telephone or face-to-face interview. Voiding function was determined as “worsened” or “maintained” respectively. Worsened was defined as patients who demonstrated increased CLSS or prolonged urinary catheterization exceeding 1 month post-operatively.

Statistical analysis

Data were described as mean ± standard deviation for measurement data, or number (%) for enumeration data. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of BCR amplitude decline rate at 50%, 75% and 100% to predict

worsening voiding function post-operatively were calculated with 95% confidence intervals. ROC curve analysis was used to determine the optimal cutoff value of BCR amplitude decline. Statistical analyses were performed using SPSS version 17.0. *P* value < 0.05 was considered statistically significant.

RESULTS

Demographics of subjects

A total of 57 patients were included in the study. Demographics and clinical characteristics are presented in Table 1. There were 33 (57.9%) males and the mean age was (51.2±15.3) years (range 19-80 years). Schwannoma (14 cases, 24.6%) was the most common diagnosis.

BCR changes and voiding function

There were 46 patients (26 males) in Group 1, 3 patients (2 males) in Group 2, 3 patients (1 male) in Group 3, and 5 patients (4 males) in Group 4. A total of 9 patients (6 males) demonstrated worsened voiding function at 1 month post-operatively, including 2 patients (2 males) in Group 1, 1 patient (0 male) in Group 2, 2 patients (0 male) in Group 3 and 4 patients (4 males) in Group 4 (Table 2).

When the warning criterion of BCR amplitude decline rate was set as 50%, the sensitivity, specificity, PPV, and NPV of BCR monitoring for worsened voiding were 77.8%, 91.7%, 63.6%, and 95.7% respectively. When the warning criterion was 75%, the sensitivity, specificity, PPV, and NPV were 66.7%, 95.8%, 75.0%, and 93.9% respectively. When the warning criterion was 100%, the sensitivity, specificity, PPV, and NPV were 44.4%, 97.9%, 80.0%, and 90.4% respectively (Table 3).

Illustrative cases

Patient 1

A 52-year-old woman diagnosed with schwannoma at L4-L5 vertebrae levels (Figure 1A) showed stable BCR at the end of surgery (Figure 1B). The amplitude showed a decrease of less than 25% on the right side and improved on the left side (Group 1). Her preoperative voiding function was normal, and it remained stable post-operatively.

Patient 2

A 40-year-old man diagnosed with intraspinal

Table 1: Demographics of patients

Demographics	
Age (year)	51.2±15.3
Male (n)	33
Diagnosis (n)	
schwannoma	14
meningioma	9
ependymoma	8
lipoma	8
epidermoid cyst	6
glioma	3
neurofibroma	3
hemangioma	2
teratoma	2
metastasis	1
hemangioblastoma	1

Table 2: Intraoperative BCR changes and postoperative voiding function

Group	Amplitude decline rate	Worsened voiding (n)	Maintained voiding (n)
1	<50%	2	44
2	≥50%, <75%	1	2
3	≥75%, <100%	2	1
4	100%	4	1

BCR, bulbocavernosus reflex

lipoma at L4-S2 vertebrae levels (Figure 2A) demonstrated unilateral loss of BCR at the end of surgery (Figure 2B). The amplitude disappeared on the right side and showed a significant decrease on the left side (Group 4). The voiding function got worse after surgery along with increased residual urine volume and intermittent catheterization was in need.

ROC curve analysis

According to the ROC curve analysis, the optimal cutoff value of BCR amplitude decline for predicting voiding function at 1 month post-operatively was 66.5%. The area under curve, sensitivity, and specificity were 0.813, 77.8% and 95.8% respectively (Figure 3).

DISCUSSION

The detailed description of BCR was reported by Bors and Blinn as early as 1959.²¹ The physical examination requires squeezing the glans penis in male or touching the labium minus lateral to the clitoris in female, while observing the contraction of bulbocavernosus and external anal sphincter. Rushworth firstly demonstrated BCR could be induced by electromyography in 1967, thus making it possible to perform qualitative and comparative research.⁶ Deletis and Vodusek

firstly described successful intraoperative BCR monitoring in patients under general anesthesia in 1997.⁵ Despite increasing attention given to intraoperative BCR monitoring since then, no settled alert criteria exist for altered intraoperative BCR and there are few reports about BCR in adult patients with lumbosacral intraspinal tumor.

The warning criterion of 50% amplitude reduction has long been applied in majority of IONM procedures. In this study, three different cutoff values of 50%, 75%, and 100% amplitude decline of BCR were analyzed. We found the sensitivity was highest at the cutoff value of 50%, and the highest specificity was demonstrated at the cutoff value of 100%. It was demonstrated that the cutoff value of 100% (all or none criterion) was a reliable predictor of voiding function post-operatively in adult patients undergoing lumbosacral intraspinal tumor surgery, in keeping with previous studies. Choi *et al.*¹⁵ found that all 3 (100%) patients without BCR response at the end of surgery experienced voiding difficulty at all the follow-up time points post-operatively. The sensitivity and specificity of intraoperative BCR monitoring for detecting voiding difficulty were both 100% 6 months post-operatively. Cha *et al.*¹⁰ demonstrated similar findings, indicating that if intraoperative BCR is present, voiding function deterioration will be unlikely to occur.

Table 3: Sensitivity, specificity, PPV, and NPV of BCR changes at specified warning criterion for postoperative voiding function with 95% confidence intervals

Warning criteria	Amplitude decline rate	Worsened voiding	Maintained voiding	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
50%	≥50%	7	4	77.8	91.7	63.6	95.7
	<50%	2	44	(40.2-96.1)	(79.1-97.3)	(31.6-87.6)	(84.0-99.2)
75%	≥75%	6	2	66.7	95.8	75.0	93.9
	<75%	3	46	(30.9-91.0)	(84.6-99.3)	(35.6-95.5)	(82.1-98.4)
100%	100%	4	1	44.4	97.9	80.0	90.4
	<100%	5	47	(15.3-77.3)	(87.5-99.9)	(29.9-98.9)	(78.2-96.4)

BCR, bulbocavernosus reflex; PPV, positive predictive value; NPV, negative predictive value

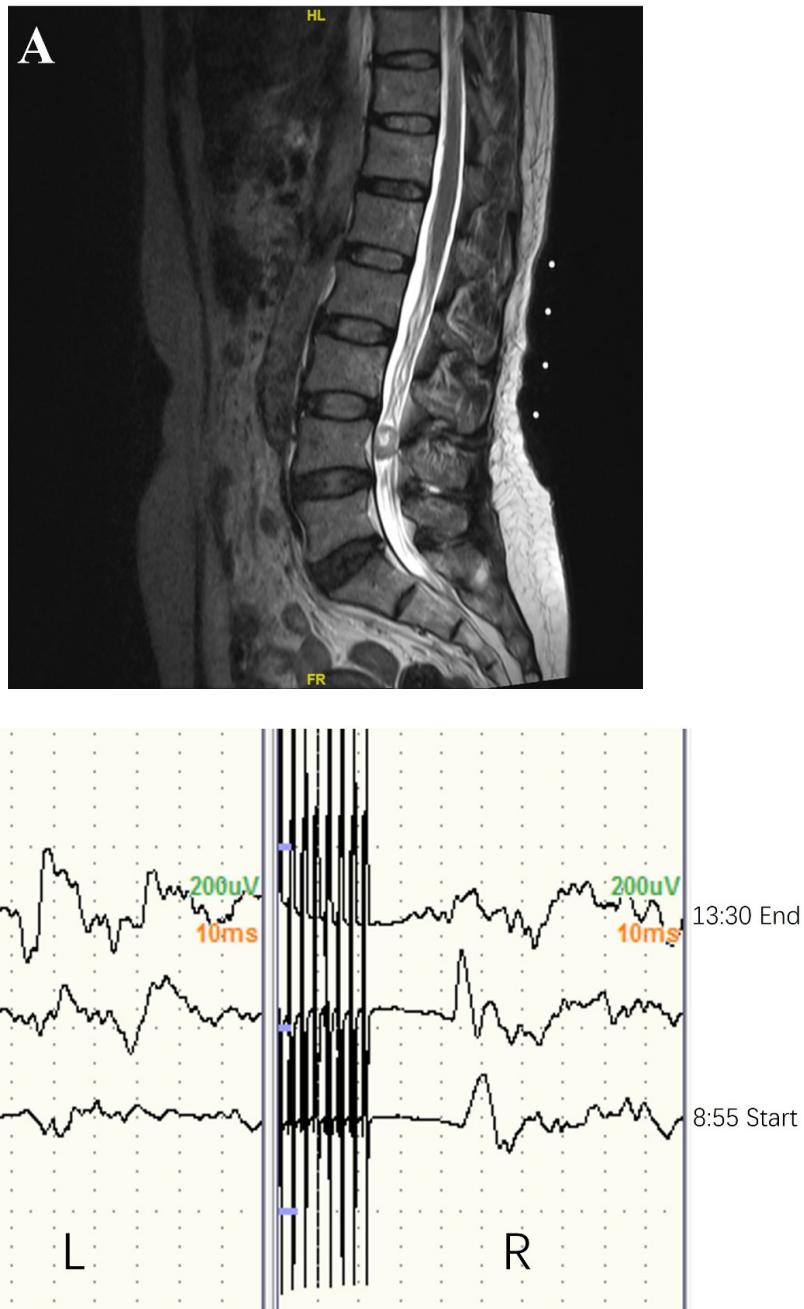


Figure 1. (A) Preoperative T2-weighted MRI showed an intradural lesion at L4-L5 vertebrae levels. (B) Intraoperative BCR monitoring. The lower waveforms indicated the baseline (8:55) and the upper ones represented the end of surgery (13:30).

BCR, bulbocavernosus reflex; MRI, magnetic resonance imaging; L, left; R, right

In this study, the 50% criterion would have resulted in a false positive rate of 8.3%, whereas the “all or none” criterion would have produced a false negative rate as high as 55.6%. An adequate alarm point should be somewhere between these two criteria. Morota¹² also proposed that the cutoff value of BCR amplitude reduction at 75% rather

than 50% and 100% may be used from a practical viewpoint. The final ROC analysis revealed the discriminating cutoff value of BCR amplitude decline in predicting voiding function at 1 month post-operatively was 66.5%, which is the key finding of this study. This cutoff of amplitude decrease can be used as a primary warning for

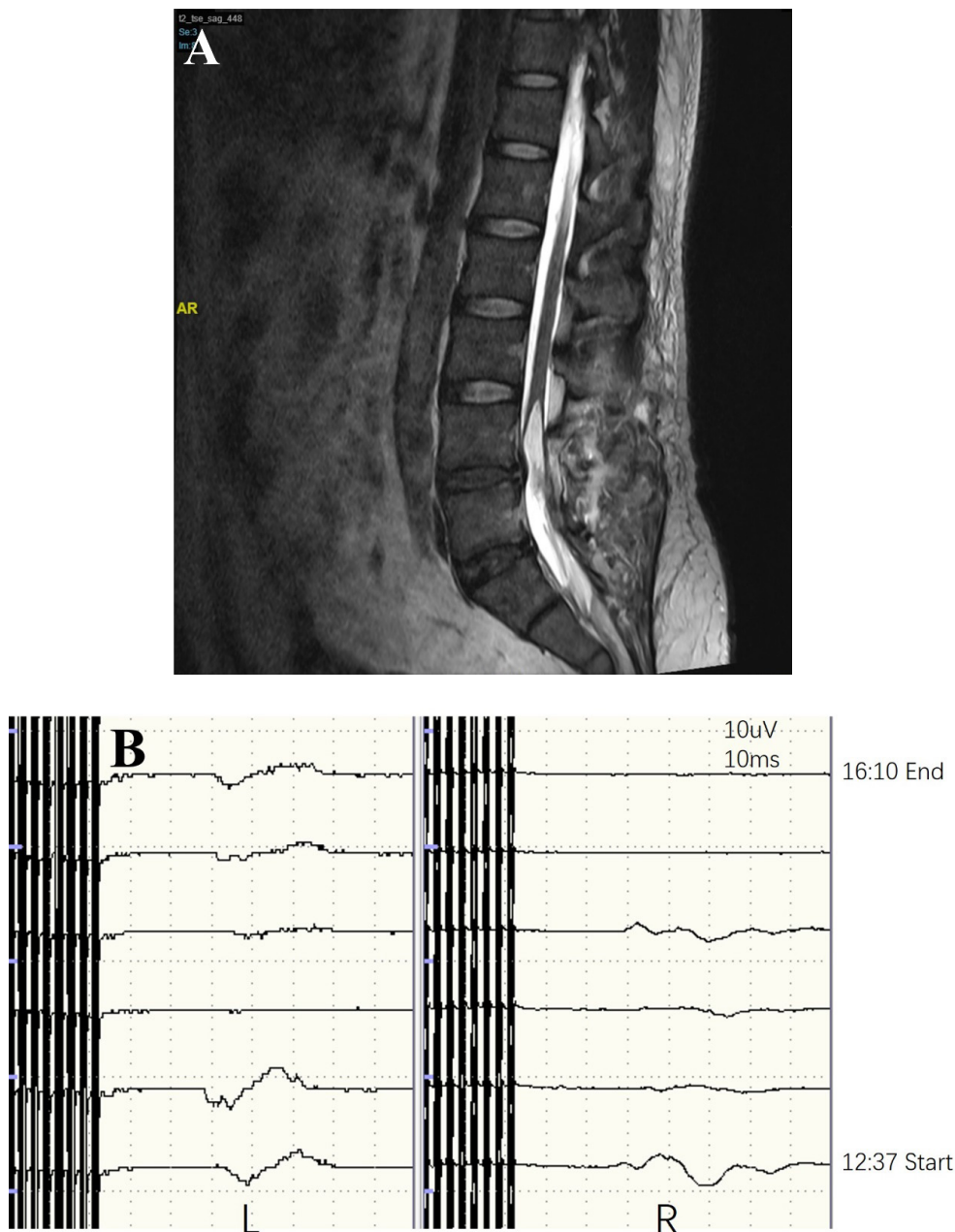


Figure 2. (A) Preoperative T2-weighted MRI showed intradural lesions at L4-S2 vertebrae levels. (B) Intraoperative BCR monitoring. The lower waveforms indicated the baseline (12:37) and the upper ones represented the end of surgery (16:10).
BCR, bulbocavernosus reflex; MRI, magnetic resonance imaging; L, left; R, right

transient loss of sphincter control before the final warning for permanent neurological deficit by the “all or none” criterion, thus contributing to improving surgery safety.

Skinner and Vodušek stated that significant diminished waveform complexity may forewarn that signal disappearance is imminent or may indicate an incomplete degree of conduction

block within the reflex circuit and informational reporting to the surgeon is recommended in such situation.⁴ A decrease in amplitude may be associated with temporary neurological deficits, while complete loss of response may imply clinical injury if not reversed. The ultimate goal of IONM is to detect nervous system damage during surgery in real time. The ideal warning criterion

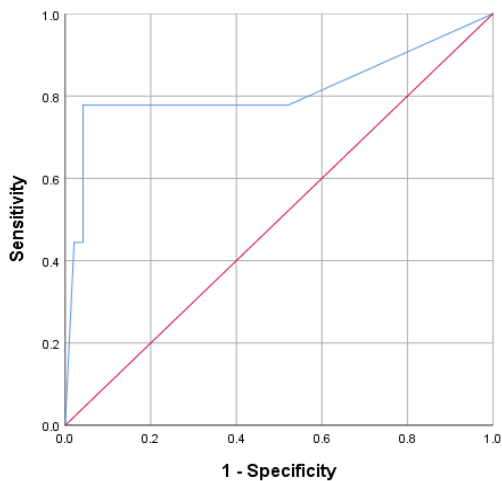


Figure 3. ROC curve analysis to determine the optimal cutoff value of BCR amplitude decline.

for IONM is usually expected to be with both high sensitivity and specificity. In surgeries with a high risk of postoperative complications, a more sensitive alarm setting would be preferred, even if it involves sacrificing some degree of specificity. Lumbosacral intraspinal tumor carries a high risk of voiding dysfunction post-operatively, so a conservative cutoff may be appropriate to increase sensitivity. However, setting the alarm criteria cutoff value too low may lead to unnecessary disruption in the standard operation process without any benefit. Actually, the balance between sensitivity and specificity is usually difficult to find.

Nine patients demonstrated worsened voiding function at 1 month post-operatively in this study. Postoperative urine retention (POUR) is a common complication with an incidence of 3% to 70% after all surgical procedures²², and there is no standard definition for POUR. Choi *et al.*¹⁵ partly attributed the early voiding dysfunction after operation to POUR in patients with lumbosacral spinal tumor. Geller proposed that the risk of prolonged POUR beyond 4 weeks was low.²³ Therefore, 1 month post-operatively in our study may be an appropriate timepoint to evaluate the voiding function with few mixed factors as much as possible. However, further investigation is needed on intraoperative BCR data and their correlation with long-term sphincter control.

The limitations of this study were firstly, the number of subjects was small and the study was performed in a single center. The warning criterion of intraoperative BCR monitoring may be different between males and females,

therefore, large sample is also needed to detect the potential gender-related difference in the future. Besides, urodynamic study was not able to be performed in our hospital due to the technological problems. Urinary questionnaire and residual urine measurement were combined as a semi-qualitative tool to evaluate the voiding function. In addition, the baseline BCR was not analyzed and the impact of amplitude reduction may differ between a patient with a high-amplitude baseline BCR and a patient with a low-amplitude baseline BCR. Lastly, it is necessary to add follow-up timepoints to explore the relationship between intraoperative BCR data and long-term voiding function.

In conclusion, intraoperative BCR monitoring is a valuable tool to be performed during surgery in adult patients with lumbosacral intraspinal tumor. The cutoff value of BCR amplitude decline rate at 100% (all or none criterion) can be used to predict postoperative voiding function, and the absence of BCR is a robust indication for poor voiding post-operatively. As a warning criterion, the cutoff value of BCR amplitude decline at 66.5% may be practical. This preliminary clinical study on the warning criterion of intraoperative BCR monitoring may contribute new perspectives for improving the safety of operations in adult patients with lumbosacral intraspinal tumor.

ACKNOWLEDGEMENTS

We would like to thank all the participants in the study.

DISCLOSURE

Financial support: This study was supported by Peking University International Hospital Research Funds (No. YN2023QN06).

Conflict of interest: None.

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